METHOD AND APPARATUS FOR FULLY AUTOMATIC AGGLUTINATION IMMUNE ANALYSIS

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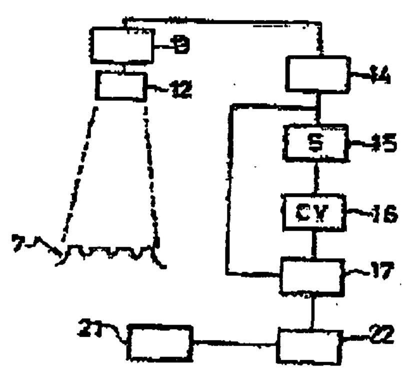
Abstract of **JP1035374**

PURPOSE:To fully automate an agglutination immune analysis by providing a detector which takes in the agglutination image of the agglutination immune reaction and a decision device which makes image processing of the image taken therein. CONSTITUTION:The agglutination image of a well 8 on a microplate 7 is picked up by a TV camera 12 under adequate illumination and is stored as a video image into an image memory 13. The stored video image is received in a decision device part. The differential image is first obtd. by an image processor 14 at this time, and further, the contour and area of the agglutination image are determined. A standard deviation S with picture elements having >=0 brightness level is obtd. by a standard deviation calculator 15; furthermore, the coefft. CV of fluctuation is obtd. by a coefft. of fluctuation calculator 16. The coefft. CV of fluctuation and the area obtd. by the image processing 14 are inputted to a plotter 17 and is compared with



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⑭発明の名称 全自動凝集免疫分析方法およびその装置

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明 細 書

1.発明の名称

全自動凝集免疫分析方法およびその装置

2.特許請求の範囲

(1) 反応容器に検体を分注し、凝集免疫試薬を加え、撹拌する前処理段階と、凝集免疫反応直後から連続的に凝集像を取り込む、または凝集免疫反応終了後に凝集像を取り込む検出段階と、得られる凝集像を画像処理して判定する判定段階と、から成り、これら前処理段階、検出段階および判定段階を連続的に行うことから成る、全自動凝集免疫分析方法。

(2) 反応容器供給装置、検体分注装置、凝集免疫試薬供給装置、撹拌装置とを有する前処理装置部と、画像取込み装置、容器回収装置とを有する検出装置部と、画像処理装置を有する判定装置部と、

から成る、全自動凝集免疫分析装置。

3.発明の詳細な説明

〔産業上の利用分野〕

本発明は、臨床検査における免疫学的な凝集反応を利用した全自動凝集免疫分析方法およびその装置に関する。

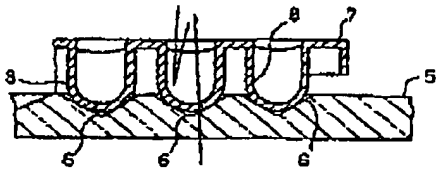
〔従来の技術〕

免疫学的な凝集反応を利用した分析方法は、特異性、感度に優れ、臨床検査の分野で汎用されている。古くは、赤血球を用いて、その凝集像から血液型の同定を行う分析方法があり、最近では赤血球に代替する新しい担体を用いて、微生物や病因性の抗原や抗体を測定する凝集免疫分析方法へと多様化している。

凝集免疫分析方法を用いる装置を自動化したものは、自動血液型判定装置(特開昭55-146044)あるいは汎用型自動分析方法および装置(特開昭57-111447、特開昭58-118838、特開昭58-22956、特開昭58-105065)等が知られている。

これらは、免疫学的凝集反応に基く一連の操作を自動化し、凝集像の測光的分析により免疫反応の有無を判定している。しかしながら、その判定

第 1 図



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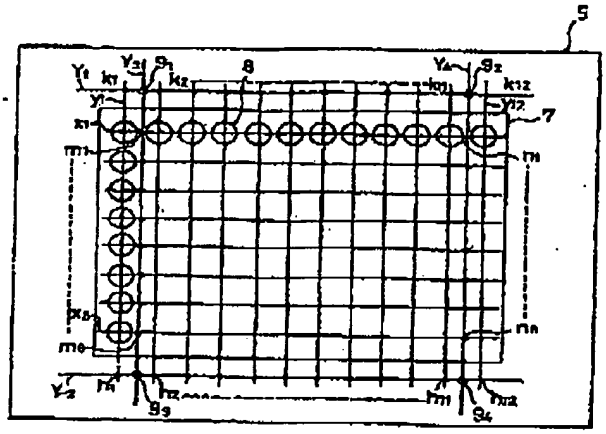

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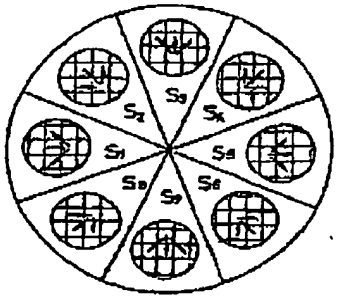

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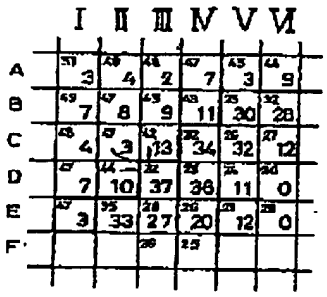

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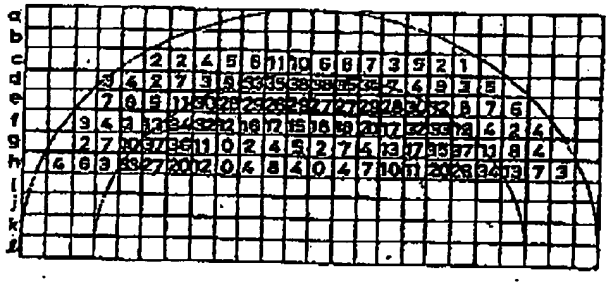

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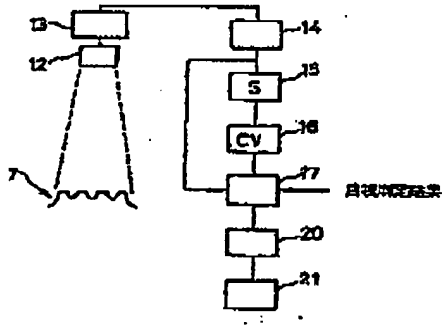

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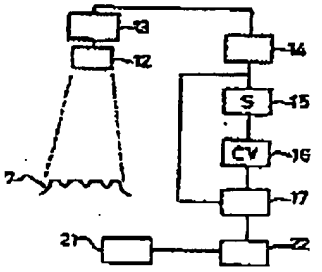

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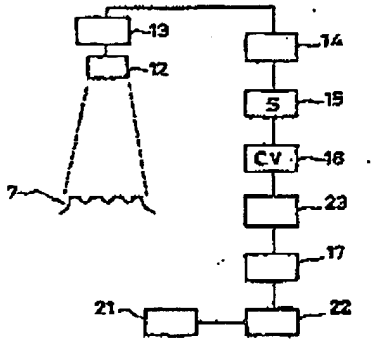

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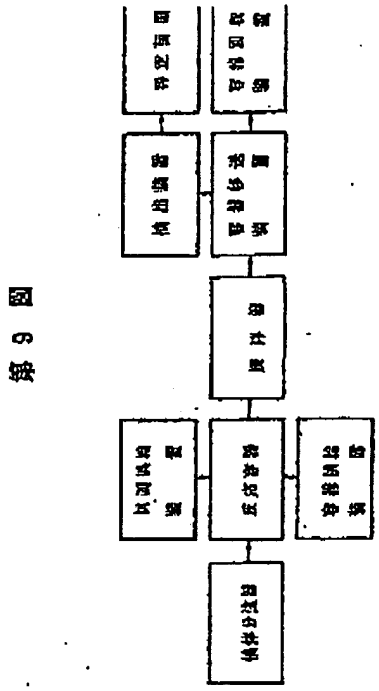

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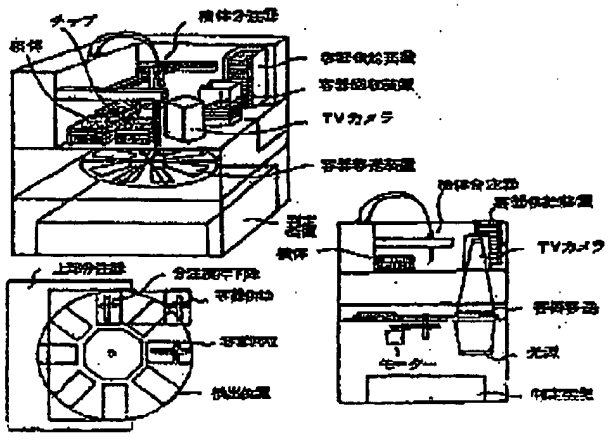

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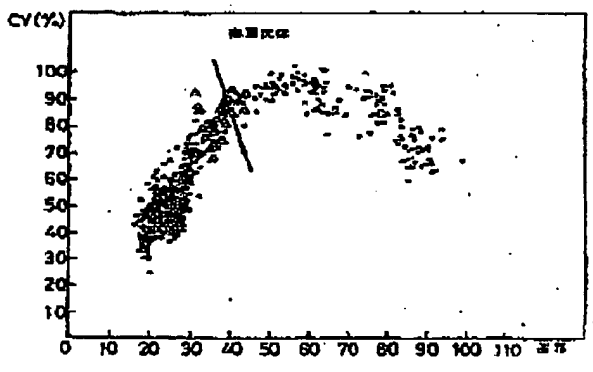

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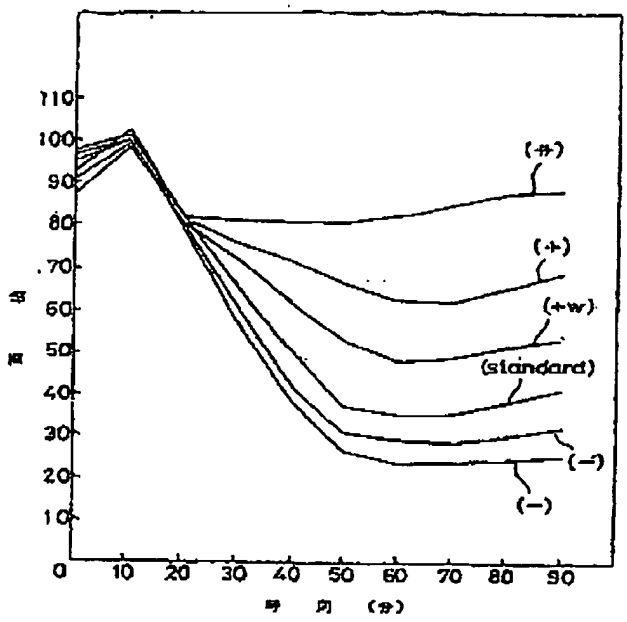

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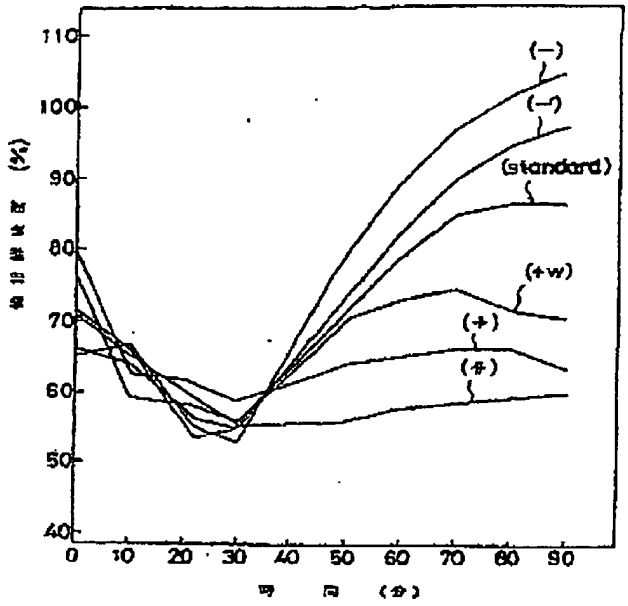

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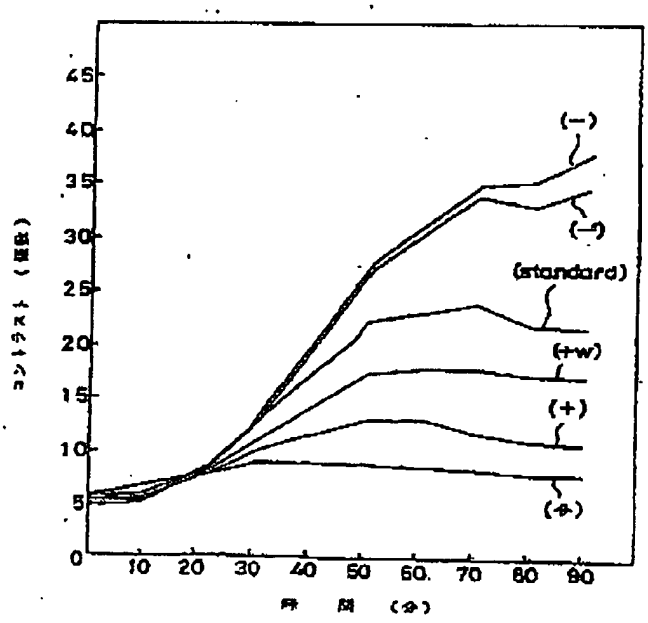


Translation in-part of Japanese Unexamined Patent Publication No. 35374/1989 (Reference 2)

Page 3, upper right column, line 15 to lower left column line 7

The detecting means according to the present invention can employ the method for processing and detecting the agglutination image which is constantly taken in just after the agglutination reaction begins and the method for processing and detecting the agglutination image which is taken when the agglutination reaction ends. For these methods, it is desirable in order to efficiently process micro plates which are transported successively that micro plates are deposited in the position for successive detection by means of a device transporting system. As the device transporting system, a system such as a turn table can be employed. By putting micro plate on the table, successive detection can be done as the table turns.

Page 3, lower right column line 7 to line 12

Means of judging the results comprises a step of determining the reference value based on the reference substrate and a step of detecting the analyte based on the reference value. In the case there are some kinds of successive image signals, the reference number should be set on more factors than when there is one kind of final image signal but the result is obtained faster than when there is one kind of final image signal.

Page 5, upper left column line 7 to the upper right column

As mentioned above, three kinds of analytical

plotted to obtain the deviation per unit time by plotting the data unchanged when there is one kind final image (case 1) or by plotting the data based on the time relation when there are some kinds of images.

Firstly, the reference number in case of the final image is set based on the above mentioned process. The reference number is set based on plural kinds of reference substrates. The reference substrates are either positive, negative, or standard (middle of positive and negative). Calculate standard deviation of the areas of the plural reference substrates, and then obtain the fluctuation coefficient of picture elements of deviation image whose luminance is not equal to zero. Plot the relation between the fluctuation coefficient and the area and results of each visual judgment for agglutination images. Store such a line as a standard that makes the overlapping area of the positive and negative of visual judgment smallest.

Analyte determination is done by plotting the data in the same manner as the reference substrates to judge whether there is agglutination or not. In the case there are some kinds of successive images, obtain deviation per unit time and set the reference value in such a manner that the deviation pre area over the value is determined to be negative and the deviation per are equal to or under the value is determined to be positive. Then measure the analyte by comparing the reference value which is obtained based on the deviation per area with the time change and it is determined whether there is agglutination or not.

Page 5, lower left column, line 9 to the lower right column line 3

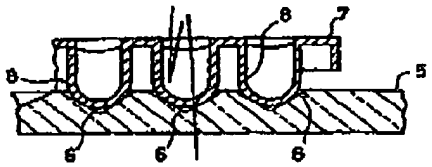
Immune analysis basically contains two methods. "Rate

method" for measuring rate of reaction at the beginnings of the reaction and "End point method" for measuring the reaction end. When the successive agglutination images are obtained, "Rate method" is used. When one final image is obtained, "End point method" is used. First reaction having large deviation is employed by "Rate method". Steady state is measure by "End point method". "Rate method" allows fast measurement but needs at least two data. On the other hand, "End point method" needs only one data and the sensitivity of the method is high, but it takes more time. According to the present invention, if the result of the measurement is needed immediately, "Rate method" can be employed by getting the successive images.

Explanation of Reference Numbers

5	stand for plates
7	micro plate
8	well
9	hole for positioning
12	TV camera
13	image memory
14	device for processing image
15	device for calculating standard deviation
16	device for calculating fluctuation coefficient
17	plotter
20	device for determining the line
21	memory
22	device for comparison
23	device for calculating contrast

第 1 図



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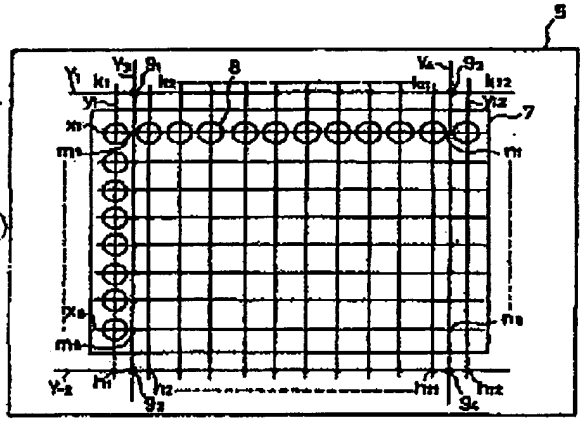

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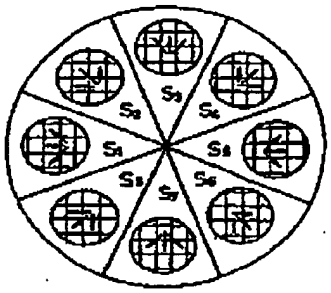

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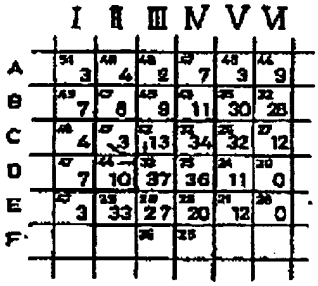

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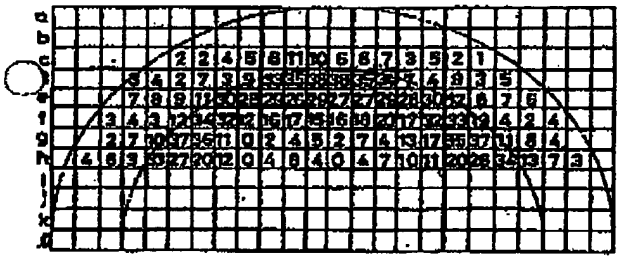

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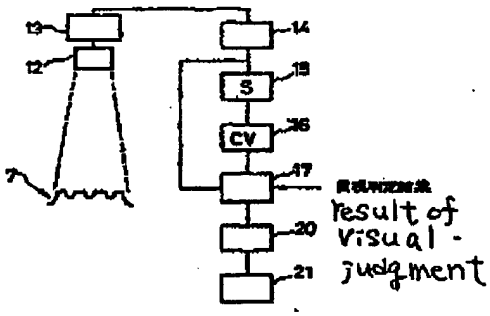

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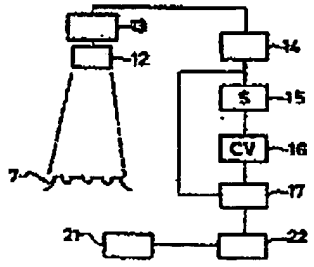

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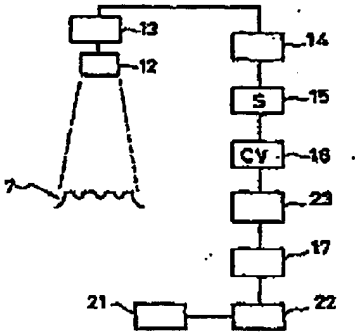

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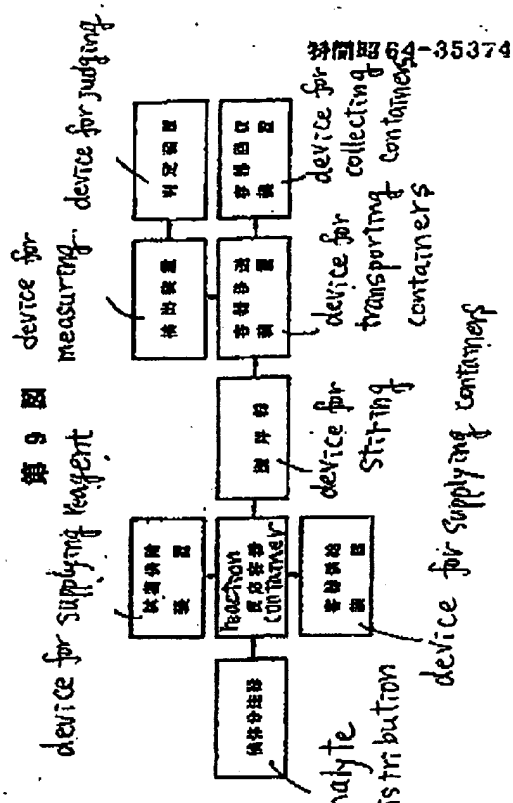

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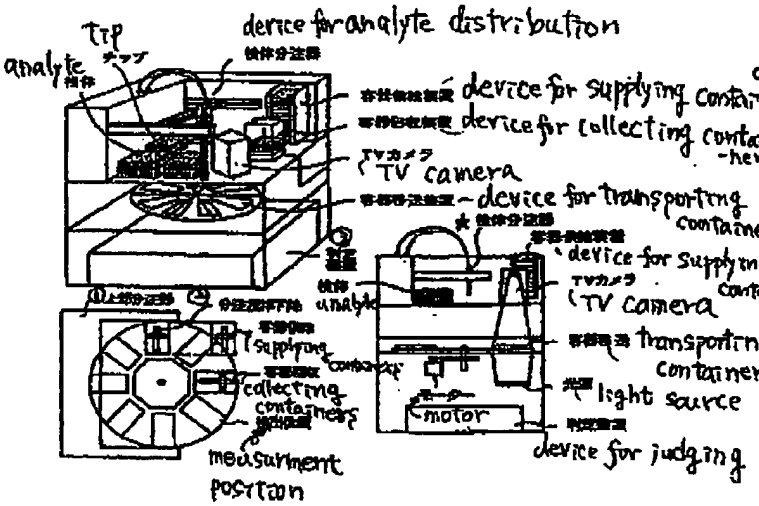

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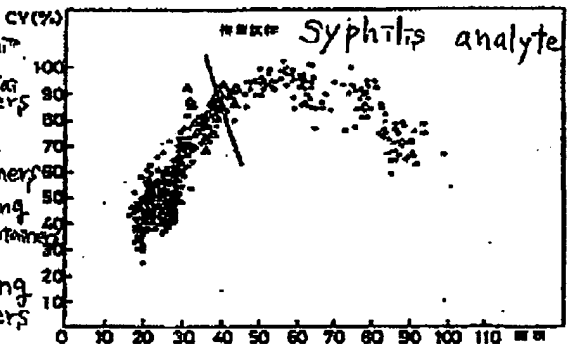
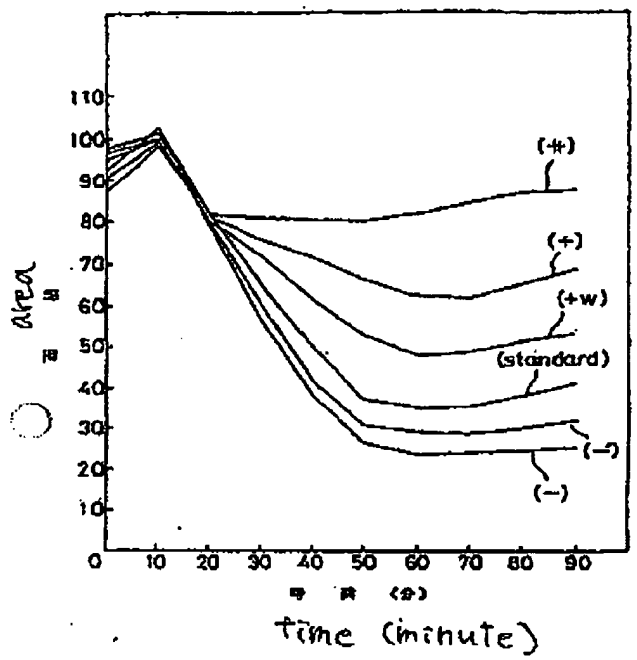


① upper device for analyte distribution * device for analyte distribution

② distributing and storing

③ device for

第 12 図



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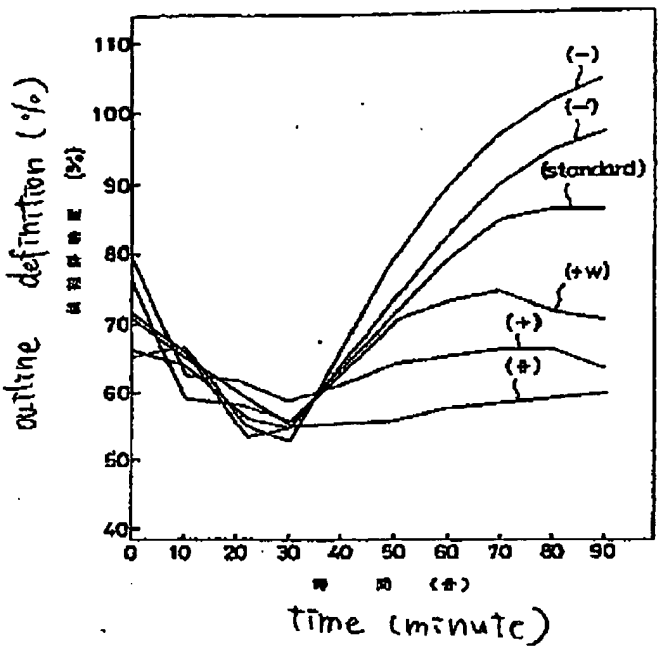

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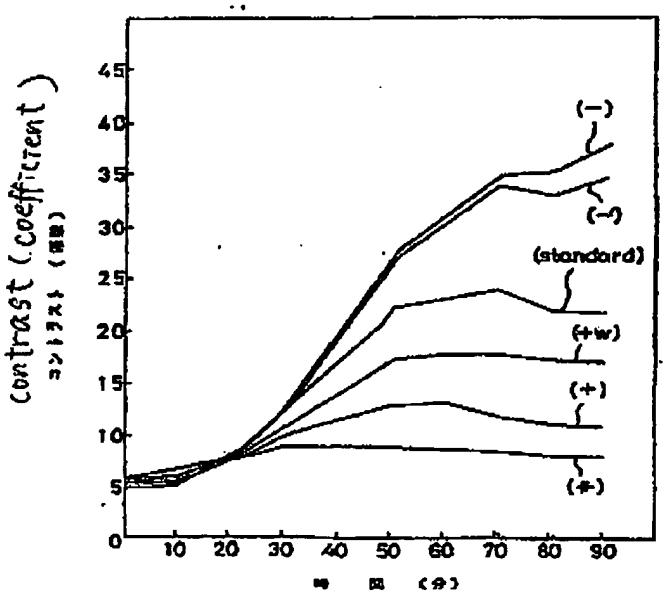

concentration analyte whose absorbance exceeds absorbance Ah in a short time and whose deviation of the absorbance cannot be measured can be determined whether it needs reduction re-examination in real time and to start re-examination. As for high concentration value analyte S3 shown in Fig.5, for example, the number of sample in the range of Ah is one. Therefore, it is determined that re-examination is needed at the time t2 and reduction re-examination is operated without delay. On the contrary, as for analyte whose final absorbance exceeds Ah, if the number of samples in the region Ah is equal to or more than 3, re-examination is not carried out because deviation is measured appropriately and deviation of absorbance in the range Ah in the same manner as normal analyte S1.

[0034]

Moreover, when analyte needs reduction re-examination, it is determined whether standard re-examination is needed or not and to start the re-examination for high concentration analyte exceeding the threshold value Ch.

[0035]

In this embodiment, system for multiple analyses which can switch End point method or Rate method is shown. However this invention can employ only one of the modes.

Explanation of Reference Numbers

1	automatic analyzer
2	analyte sampling table
3	reagent distribution table